Claims

1. An isolated and purified protective peptide capable of inhibiting an invasive and/or non-invasive infection of Gram-positive pathogenic bacteria, which peptide comprises an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605.

2. The peptide according to claim 1, wherein said peptide comprises an amino acid sequence substantially as denoted by SEQ ID NO: 32 or any functional fragment, analog or derivative thereof.

3. The peptide according to claim 2, wherein said Gram-positive pathogenic bacteria is *Streptococcus sp.* selected from the group consisting of Group A *Streptococcus* (GAS) bacteria, Group B *Streptococcus* bacteria and Group G *Streptococcus* bacteria.

4. The peptide according to claim 3, wherein said peptide is capable of inhibiting the spreading of GAS bacteria and/or tissue necrosis and/or lethal effect caused by said bacteria.

5. The peptide according to claim 1, wherein said invasive infection leads to any one of soft tissue infection, bacteremia, septicemia, toxic shock syndrome (TSS) and necrotizing fasciitis (NF) and the non-invasive infection leads to any one of rheumatic fever and acute glomerulonephritis.

6. The peptide according to claim 5, wherein said GAS bacteria is any one of *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Staphylococcus aureus* and oral *Streptococci*.

7. The peptide according to claim 6, wherein said GAS bacteria is a virulent strain of *Streptococcus pyogenes*.

8. The peptide according to claim 2, wherein said peptide or any fragment, analog or derivatives thereof is in the form of a dimer, a multimer or in a constrained conformation.

9. The peptide according to claim 8, which is conformationally constrained by internal bridges, short-range cyclization, extension or other chemical modification.

10. A method of inhibiting an invasive and/or non-invasive infection of Gram-positive pathogenic bacteria in a mammalian subject, comprising administering to said subject an inhibitory effective amount of an isolated and purified peptide or of a composition comprising the same, which peptide comprises an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605 or any functional fragment, analog or derivative thereof.

11. A method of preventing and/or treating a Gram-positive bacteria invasive infection related pathologic disorder comprising administering to a mammalian subject in need of such treatment a therapeutically effective amount of an isolated and purified peptide or of a composition

comprising the same, which peptide comprises an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605 or any functional fragment, analog or derivative thereof.

12. The method according to any one of claims 10 and 11, wherein said peptide comprises an amino acid sequence substantially as denoted by SEQ ID NO: 32 or any functional fragment, analog or derivative thereof.

13. The method according to claim 12, wherein said Gram-positive bacteria is *Streptococcus sp* . selected from the group consisting of Group A *Streptococcus* (GAS) bacteria, Group B *Streptococcus* bacteria and Group B *Streptococcus* bacteria.

14. The method according to claim 13, wherein said peptide is capable of inhibiting the spreading of GAS bacteria and/or tissue necrosis and/or lethal effect caused by said bacteria.

15. The method according to claim 10, wherein said invasive infection leads to any one of soft tissue infection, bacteremia, septicemia, toxic shock syndrome (TSS) and necrotizing fasciitis (NF) and the non-invasive infection leads to any one of rheumatic fever and acute glomerulonephritis.

16. The method according to claim 14, wherein said GAS bacteria is any one of *Streptococcus pyogenes, Streptococcus pneumoniae, Staphylococcus aureus* and oral *Streptococci.*

17. The method according to claim 16, wherein said GAS bacteria is a virulent strain of *Streptococcus pyogenes*.

18. The method according to claim 17, wherein said peptide or any fragment, analog or derivatives thereof is in the form of a dimer, a multimer or in a constrained conformation.

19. The method according to claim 18, wherein said peptide is conformationally constrained by internal bridges, short-range cyclization, extension or other chemical modification.

20. The method according to claim 11, wherein said GAS invasive infection related pathologic disorder is any one of soft tissue infection, bacteremia, septicemia, toxic shock syndrome (TSS) and necrotizing fasciitis (NF), and the non-invasive infection leads to any one of rheumatic fever and acute glomerulonephritis.

21. The method according to any one of claims 10 to 20, wherein the effective amount of said peptide or of a composition comprising the same is administered to said subject prior to potential exposure to said pathogenic bacteria.

22. The method according to any one of claims 10 to 20, wherein the effective amount of said peptide or of a composition comprising the same is administered to said subject in any one of a single dose and multiple doses.

23. The method according to claim 22, wherein the effective amount of said peptide or of a composition comprising the same is administered to

said subject by any one of a single route and at least two different routes of administration.

24. The method according to claim 23, wherein the effective amount of said peptide or of a composition comprising the same is administered to said subject by at least one route selected from oral, intravenous, parenteral, transdermal, subcutaneous, intravaginal, intranasal, mucosal, sublingual, topical and rectal administration and any combinations thereof.

25. The method according to claim 24, wherein the effective amount of said peptide or of a composition comprising the same is administered to said subject subcutaneously.

26. The method according to any one of claims 10 to 19, wherein an effective amount of said peptide is between 0.5μg/kg to 100mg/kg of body weight.

27. The method according to claim 26, wherein an effective amount of said peptide is between 10μg/kg to 10mg/kg of body weight.

28. The method according to claim 27, wherein an effective amount of said peptide is between 300μg/kg to 5mg/kg.

29. The method according to any one of claims 10 to 19, wherein said mammalian subject is a human patient.

30. A method of disinfecting an environment and/or preventing infection caused by Gram-positive bacteria, comprising the step of applying a sufficient amount of an isolated and purified peptide or of a

composition comprising the same, onto a surface of any one of medical equipment, medical devices and disposables, which peptide comprises an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605or any functional fragment, analog or derivative thereof.

31. The method according to claim 30, wherein said peptide is as defined by the method according to any one of claims 12, 14, 18 and 19.

32. Use of an isolated and purified peptide comprising an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605 or any functional fragment, analog or derivative thereof, as an agent for inhibiting the invasive and non-invasive infection of a Gram-positive pathogenic bacteria.

33. Use according to claim 32, wherein said peptide comprises an amino acid sequence substantially as denoted by SEQ ID NO: 32 or any functional fragment, analog or derivative thereof.

34. Use of an isolated and purified peptide comprising an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605 or any functional fragment, analog or derivative thereof, in

the preparation of a pharmaceutical composition for the treatment and/or prevention of a GAS invasive infection related pathologic disorder, which composition optionally further comprises pharmaceutically acceptable carrier, diluent, adjuvant and/or excipient.

35. The use according to claim 34, wherein said peptide comprises an amino acid sequence substantially as denoted by SEQ ID NO: 32 or any functional fragment, analog or derivative thereof.

36. The use according to claim 35, wherein said GAS invasive infection related pathologic disorder is any one of soft tissue infection, bacteremia, septicemia, toxic shock syndrome (TSS) and necrotizing fasciitis (NF), and the non-invasive infection leads to any one of rheumatic fever and acute glomerulonephritis.

37. The use according to any one of claims 32 and 34, wherein said bacteria is *Streptococcus sp.* selected from the group consisting of Group A *Streptococcus* (GAS) bacteria, Group B *Streptococcus* bacteria and Group G *Streptococcus* bacteria.

38. The use according to claim 37, wherein said peptide is capable of inhibiting the spreading of GAS bacteria and/or tissue necrosis and/or lethal effect caused by said bacteria.

39. The use according to claim 38, wherein said GAS bacteria is any one of *Streptococcus pyogenes, Stre ptococcus pneumoniae, Staphylococcus aureus* and oral *Streptococci.*

40. The use according to claim 39, wherein said GAS bacteria is a virulent strain of *Streptococcus pyogenes*.

41. The use according to claim 40, wherein said peptide or any fragment, analog or derivatives thereof is in the form of a dimer, a multimer or in a constrained conformation.

42. The use according to claim 41, which is conformationally constrained by internal bridges, short-range cyclization, extension or other chemical modification.

43. An isolated and purified protective peptide comprising an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605, for use in the inhibition of invasive and/or non-invasive infection of Gram-positive pathogenic bacteria.

44. An isolated and purified protective peptide comprising an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605, for use in the treatment and/or prevention of a GAS invasive infection related pathologic disorder.

45. The peptide according to claim 44, wherein said GAS invasive infection related pathologic disorder is any one of soft tissue infection, bacteremia, septicemia, toxic shock syndrome (TSS) and necrotizing

fasciitis (NF), and the non-invasive infection leads to any one of rheumatic fever and acute glomerulonephritis.

46. An isolated and purified protective peptide comprising an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605, for use in disinfecting and preventing infection caused by a Gram positive bacteria.

47. The peptide according to any one of claims 43, 44 and 46, wherein said peptide comprises an amino acid sequence substantially as denoted by SEQ ID NO: 32 or any functional fragment, analog or derivative thereof.

48. A composition for the inhibition of invasive and/or non-invasive infection of Gram-positive pathogenic bacteria, comprising as an active ingredient an isolated and purified peptide as defined by any one of claims 1 to 9, in an effective amount to inhibit spreading, tissue necrosis and/or lethal effect caused by said bacteria.

49. A pharmaceutical composition for the treatment and/or prevention of a GAS invasive infection related pathologic disorder comprising as an active ingredient an isolated and purified peptide as defined by any one of claims 1 to 9.

50. The composition according to any one of claims 48 and 49, wherein said peptide comprises an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of

the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605, which composition optionally further comprises pharmaceutically acceptable carrier, diluent, adjuvant and/or excipient.

51. Use of an agent, which induces down regulation and/or inhibition of chemokine protease activity, for inhibiting invasive and/or non-invasive infection by Gram-positive pathogenic bacteria.

52. Use of an agent which induces down regulation and/or inhibition of chemokine protease activity, in the preparation of a pharmaceutical composition for the treatment and/or prevention of a GAS invasive infection related pathologic disorder, which composition optionally further comprises pharmaceutically acceptable carrier, diluent, adjuvant and/or excipient.

53. The use according to any one of claims 51 and 52, wherein said agent is a purified protective peptide comprising an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605.

54. The use according to claim 53, wherein said peptide comprises an amino acid sequence substantially as denoted by SEQ ID NO: 32 or any functional fragment, analog or derivative thereof.

55. The use according to any one of claims 51 and 52, wherein said agent is an inhibitor of a serine protease.

56. The use according to claim 55, wherein said serine protease inhibitor is selected from the group consisting of aprotenin, trypsin inhibitor, chemotrypsin inhibitor, plasmin inhibitor, kallikrein inhibitor, benzamidine and soybean trypsin inhibitor.

57. A method of inhibiting an invasive and/or non-invasive infection of Gram-positive pathogenic bacteria in a mammalian subject, comprising administering to said subject an inhibitory effective amount of an agent which induces down regulation and/or inhibition of chemokine protease activity.

58. A method of preventing and/or treating a GAS invasive infection related pathologic disorder comprising administering to a mammalian subject in need of such treatment a therapeutically effective amount of an agent which induces down regulation and/or inhibition of chemokine protease activity.

59. The method according to any one of claims 57 and 58, wherein said agent is a purified protective peptide comprising an amino acid sequence substantially homologous to the amino acid sequence encoded by the SilCR ORF of the *sil* locus at position 2985 to 2863 of the complementary strand of the genomic sequence of Group A *Streptococcus* (GAS) bacteria specified in GenBank accession number AF493605.

60. The method according to claim 59, wherein said peptide comprises an amino acid sequence substantially as denoted by SEQ ID NO: 32 or any functional fragment, analog or derivative thereof.

61. The method according to any one of claims 57 and 58, wherein said agent is an inhibitor of a serine protease.

62. The method according to claim 61, wherein said serine protease inhibitor is selected from the group consisting of aprotenin, trypsin inhibitor, chemotrypsin inhibitor, plasmin inhibitor, kallikrein inhibitor, benzamidine and soybean trypsin inhibitor.